

We claim:

1. A method of enhancing collateral blood vessel formation which comprises the step of directly administering to a desired site an effective amount of autologous bone marrow.

5 2. The method of Claim 1, wherein the autologous bone marrow is injected.

3. The method of Claim 1, wherein the autologous bone marrow is injected intramyocardially.

4. The method of Claim 3, wherein the autologous bone marrow is injected trans-epicardially or trans-endocardially.

10 5. The method of Claim 4, wherein with the trans-endocardial approach a catheter-based approach is used.

6. The method of Claim 1, wherein the autologous bone marrow is injected peripherally into the limb intramuscularly.

15 7. The method of Claim 1, wherein the autologous bone marrow has been stimulated.

8. The method of Claim 7, wherein the autologous bone marrow has been stimulated by contact with one or more cytokines or other proteins or stimulating agents.

9. The method of Claim 7, wherein the cytokines are selected from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

20 10. The method of Claim 7, wherein the autologous bone marrow has been transfected with vectors carrying relevant genes.

11. The method of Claim 10, wherein the autologous bone marrow has been transfected with a plasmid vector or an adenoviral vector, or any other vector demonstrated to be effective for gene transfer, carrying the HIF-1 or EPAS1 transgene, or any other transgene demonstrated to be effective in enhancing the capacity of bone marrow to induce angiogenesis.

12. The method of Claim 7, wherein the autologous bone marrow has been stimulated by transient exposure to hypoxia or a form of energy.

13. The method of Claim 7, wherein conditioned medium derived from autologous bone marrow growing in culture is injected into the ischemic heart or limb.

14. The method of Claim 1, wherein the autologous bone marrow is administered in combination with a pharmacological drug, protein, or gene or any other compound or therapy that may enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation, migration, or blood vessel formation.

15. The method of Claim 14, wherein the autologous bone marrow and the other agent or agents are administered together.

16. The method of Claim 14, wherein the autologous bone marrow and the other agent or agents are combined prior to administration.

17. The method of Claim 16, wherein the autologous bone marrow has been stimulated.

18. The method of Claim 1, wherein ischemic tissue is treated.

19. A method of promoting the development of newly implanted myocardial cells which comprises the step of directly administering an effective amount of autologous bone marrow.

20. The method of Claim 19, wherein the autologous bone marrow is injected.

21. The method of Claim 19, wherein the autologous bone marrow is injected intramyocardially.

22. The method of Claim 21, wherein the autologous bone marrow is injected
5 trans-epicardially or trans-endocardially.

23. The method of Claim 22, wherein with the trans-endocardial approach a catheter-based approach is used.

24. The method of Claim 19, wherein the autologous bone marrow is injected peripherally into the limb intramuscularly.

10 25. The method of Claim 19, wherein the autologous bone marrow has been stimulated.

26. The method of Claim 25, wherein the autologous bone marrow has been stimulated by contact with one or more cytokines or other proteins or stimulating agents.

15 27. The method of Claim 25, wherein the cytokines are selected from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

28. The method of Claim 25, wherein the autologous bone marrow has been transfected with vectors carrying relevant genes.

20 29. The method of Claim 28, wherein the autologous bone marrow has been transfected with a plasmid vector or an adenoviral vector, or any other vector demonstrated to be effective for gene transfer, carrying the HIF-1 or EPAS1 transgene, or any other transgene demonstrated to be effective in enhancing the capacity of bone marrow to induce angiogenesis.

30. The method of Claim 25, wherein the autologous bone marrow has been stimulated by transient exposure to hypoxia or a form of energy.

31. The method of Claim 25, wherein conditioned medium derived from autologous bone marrow growing in culture is injected into the ischemic heart or limb.

5 32. The method of Claim 19, wherein the autologous bone marrow is administered in combination with a pharmacological drug, protein, or gene or any other compound or therapy that may enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation, migration, or blood vessel formation.

10 33. The method of Claim 32, wherein the autologous bone marrow and the other agent or agents are administered together.

34. The method of Claim 32, wherein the autologous bone marrow and the other agent or agents are combined prior to administration.

35. The method of Claim 34, wherein the autologous bone marrow has been stimulated.

15 36. A method of improving the electrical conductivity of the heart of a patient with cardiac electrical pathway impairment, which comprises the step of administering an effective amount of autologous bone marrow.

37. The method of Claim 36, wherein the autologous bone marrow is injected.

20 38. The method of Claim 36, wherein the autologous bone marrow is injected intramyocardially.

39. The method of Claim 38, wherein the autologous bone marrow is injected trans-epicardially or trans-endocardially.

40. The method of Claim 39, wherein with the trans-endocardial approach a catheter-based approach is used.

41. The method of Claim 36, wherein with the trans-endocardial approach the autologous bone marrow is injected peripherally into the limb intramuscularly.

5 42. The method of Claim 36, wherein the autologous bone marrow has been stimulated.

43. The method of Claim 42, wherein the autologous bone marrow has been stimulated by contact with one or more cytokines or other proteins or stimulating agents.

10 44. The method of Claim 42, wherein the cytokines are selected from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

45. The method of Claim 42, wherein the autologous bone marrow has been transfected with vectors carrying relevant genes.

15 46. The method of Claim 45, wherein the autologous bone marrow has been transfected with a plasmid vector or an adenoviral vector, or any other vector demonstrated to be effective for gene transfer, carrying the HIF-1 or EPAS1 transgene, or any other transgene demonstrated to be effective in enhancing the capacity of bone marrow to induce angiogenesis.

47. The method of Claim 42, wherein the autologous bone marrow has been stimulated by transient exposure to hypoxia or a form of energy.

20 48. The method of Claim 42, wherein conditioned medium derived from autologous bone marrow growing in culture is injected into the ischemic heart or limb.

49. The method of Claim 36, wherein the autologous bone marrow is administered in combination with a pharmacological drug, protein, or gene or any other

compound or therapy that may enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation, migration, or blood vessel formation.

50. The method of Claim 49, wherein the autologous bone marrow and the other agent or agents are administered together.

5 51. The method of Claim 49, wherein the autologous bone marrow and the other agent or agents are combined prior to administration.

52. The method of Claim 51, wherein the autologous bone marrow has been stimulated.

53. A method of enhancing myocardial function in a patient with impaired
10 myocardial function, which comprises the step of administering an effective amount of autologous bone marrow.

54. The method of Claim 53, wherein the autologous bone marrow is injected.

55. The method of Claim 53, wherein the autologous bone marrow is injected intramyocardially.

15 56. The method of Claim 55, wherein the autologous bone marrow is injected trans-epicardially or trans-endocardially.

57. The method of Claim 56, wherein with the trans-endocardial approach a catheter-based approach is used.

58. The method of Claim 53, wherein the autologous bone marrow is injected
20 peripherally into the limb intramuscularly.

59. The method of Claim 53, wherein the autologous bone marrow has been stimulated.

60. The method of Claim 59, wherein the autologous bone marrow has been stimulated by contact with one or more cytokines or other proteins or stimulating agents.

61. The method of Claim 59, wherein the cytokines are selected from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

5 62. The method of Claim 59, wherein the autologous bone marrow has been transfected with vectors carrying relevant genes.

63. The method of Claim 62, wherein the autologous bone marrow has been transfected with a plasmid vector or an adenoviral vector, or any other vector demonstrated to be effective for gene transfer, carrying the HIF-1 or EPAS1 transgene, or any other
10 transgene demonstrated to be effective in enhancing the capacity of bone marrow to induce angiogenesis.

64. The method of Claim 59, wherein the autologous bone marrow has been stimulated by transient exposure to hypoxia or a form of energy.

65. The method of Claim 59, wherein conditioned medium derived from
15 autologous bone marrow growing in culture is injected into the ischemic heart or limb.

66. The method of Claim 53, wherein the autologous bone marrow is administered in combination with a pharmacological drug, protein, or gene or any other compound or therapy that may enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation, migration, or blood vessel formation.

20 67. The method of Claim 66, wherein the autologous bone marrow and the other agent or agents are administered together.

68. The method of Claim 66, wherein the autologous bone marrow and the other agent or agents are combined prior to administration.

69. The method of Claim 68, wherein the autologous bone marrow has been stimulated.

70. A method of treating an atrial or ventricular condition in the heart of a patient, which comprises the step of administering an effective amount of autologous bone marrow.

71. The method of Claim 70, wherein the autologous bone marrow is injected.

72. The method of Claim 70, wherein the autologous bone marrow is injected intramyocardially.

73. The method of Claim 72, wherein the autologous bone marrow is injected trans-epicardially or trans-endocardially.

74. The method of Claim 73, wherein with the trans-endocardial approach a catheter-based approach is used.

75. The method of Claim 70, wherein the autologous bone marrow is injected peripherally into the limb intramuscularly.

76. The method of Claim 70, wherein the autologous bone marrow has been stimulated.

77. The method of Claim 76, wherein the autologous bone marrow has been stimulated by contact with one or more cytokines or other proteins or stimulating agents.

78. The method of Claim 76, wherein the cytokines are selected from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

79. The method of Claim 76, wherein the autologous bone marrow has been transfected with vectors carrying relevant genes.

80. The method of Claim 79, wherein the autologous bone marrow has been transfected with a plasmid vector or an adenoviral vector, or any other vector demonstrated to be effective for gene transfer, carrying the HIF-1 or EPAS1 transgene, or any other transgene demonstrated to be effective in enhancing the capacity of bone marrow to induce angiogenesis.

81. The method of Claim 76, wherein the autologous bone marrow has been stimulated by transient exposure to hypoxia or a form of energy.

82. The method of Claim 76, wherein conditioned medium derived from autologous bone marrow growing in culture is injected into the ischemic heart or limb.

83. The method of Claim 70, wherein the autologous bone marrow is administered in combination with a pharmacological drug, protein, or gene or any other compound or therapy that may enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation or migration, or blood vessel formation.

84. The method of Claim 83, wherein the autologous bone marrow and the other agent or agents are administered together.

85. The method of Claim 83, wherein the autologous bone marrow and the other agent or agents are combined prior to administration.

86. The method of Claim 85, wherein the autologous bone marrow has been stimulated.

87. A composition for the treatment of a cardiac or myocardial condition, which comprises an effective amount of autologous bone marrow, wherein the cardiac or myocardial condition is treated.

88. The composition of Claim 87, wherein the autologous bone marrow has been stimulated.

89. The composition of Claim 88, wherein the autologous bone marrow has been stimulated by contact with one or more cytokines or other proteins or stimulating agents.

5 90. The composition of Claim 89, wherein the cytokines are selected from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

91. The composition of Claim 88, wherein the autologous bone marrow has been transfected with vectors carrying relevant genes.

92. The composition of Claim 91, wherein the autologous bone marrow has been
10 transfected with a plasmid vector or an adenoviral vector, or any other vector demonstrated to be effective for gene transfer, carrying the HIF-1 or EPAS1 transgene, or any other transgene demonstrated to be effective in enhancing the capacity of bone marrow to induce angiogenesis.

93. The composition of Claim 89, wherein the autologous bone marrow has been
15 stimulated by exposure to hypoxia.

94. The composition of Claim 89, wherein conditioned medium derived from autologous bone marrow growing in culture is injected into the ischemic heart or limb.

95. The composition of Claim 87, wherein the autologous bone marrow is administered in combination with a pharmacological drug, protein, or gene or any other
20 compound or therapy that may enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation, migration, or blood vessel formation.

96. The composition of Claim 87 which comprises heparin or another anticoagulant.

97. The composition of Claim 87 for enhancing collateral blood vessel formation.

98. The composition of Claim 87 for promoting the development of newly implanted myocardial cells.

5 99. The composition of Claim 87 for improving the electrical conductivity of the heart of a patient with cardiac electrical pathway impairment.

100. The composition of Claim 87 for enhancing the myocardial function in a patient with impaired myocardial function.

10 101. The composition of Claim 87 for treating a left or right ventricular condition causing impaired heart function in the heart of a patient.

102. The composition of Claim 87 for affecting the contractility of a patient's heart.